JAMA | Review

Evaluation and Treatment of Knee Pain
A Review

Vicky Duong, DPT, PhD; Win Min Oo, MD, PhD; Changhai Ding, MD, PhD; Adam G. Culvenor, PT, PhD; David J. Hunter, MD, PhD

IMPORTANCE Approximately 5% of all primary care visits in adults are related to knee pain. Osteoarthritis (OA), patellofemoral pain, and meniscal tears are among the most common causes of knee pain.

OBSERVATIONS Knee OA, affecting an estimated 654 million people worldwide, is the most likely diagnosis of knee pain in patients aged 45 years or older who present with activity-related knee joint pain with no or less than 30 minutes of morning stiffness (95% sensitivity; 69% specificity). Patellofemoral pain typically affects people younger than 40 years who are physically active and has a lifetime prevalence of approximately 25%. The presence of anterior knee pain during a squat is approximately 91% sensitive and 50% specific for patellofemoral pain. Meniscal tears affect an estimated 12% of the adult population and can occur following acute trauma (eg, twisting injury) in people younger than 40 years. Alternatively, a meniscal tear may be a degenerative condition present in patients with knee OA who are aged 40 years or older. The McMurray test, consisting of concurrent knee rotation (internal or external to test lateral or medial meniscus, respectively) and extension (61% sensitivity; 84% specificity), and joint line tenderness (83% sensitivity; 83% specificity) assist diagnosis of meniscal tears. Radiographic imaging of all patients with possible knee OA is not recommended. First-line management of OA comprises exercise therapy, weight loss (if overweight), education, and self-management programs to empower patients to better manage their condition. Surgical referral for knee joint replacement can be considered for patients with end-stage OA (ie, no or minimal joint space with inability to cope with pain) after using all appropriate conservative options. For patellofemoral pain, hip and knee strengthening exercises in combination with foot orthoses or patellar taping are recommended, with no indication for surgery. Conservative management (exercise therapy for 4-6 weeks) is also appropriate for most meniscal tears. For severe traumatic (eg, bucket-handle) tears, consisting of displaced meniscal tissue, surgery is likely required. For degenerative meniscal tears, exercise therapy is first-line treatment; surgery is not indicated even in the presence of mechanical symptoms (eg, locking, catching).

CONCLUSIONS AND RELEVANCE Knee OA, patellofemoral pain, and meniscal tears are common causes of knee pain, can be diagnosed clinically, and can be associated with significant disability. First-line treatment for each condition consists of conservative management, with a focus on exercise, education, and self-management.

JAMA. 2023;330(16):1568-1580. doi:10.1001/jama.2023.19675

Multimedia

CME at jamacmelookup.com

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: David J. Hunter, MD, PhD, Rheumatology Department, Royal North Shore Hospital, and Sydney Musculoskeletal Health, Kolling Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW 2065, Australia (david.hunter@sydney.edu.au).

Section Editor: Mary McGrae McDermott, MD, Deputy Editor.

Knee pain accounts for approximately 5% of all general practice presentations.[1] Three of the most common causes of knee pain globally are osteoarthritis (OA) (654 million individuals or 23% of adults aged >40 years),[2] patellofemoral pain (PFP) (lifetime prevalence of approximately 25%),[3] and meniscal tears (620 million adults or 12% of the general adult population).[4] This Review summarizes current evidence regarding the diagnosis and treatment of these knee conditions (**Box**).

Methods

Literature searches of PubMed were performed for English-language studies published between August 2013 and August 2023, using title key words for articles relevant to knee OA, PFP, and meniscal injuries. References of selected articles were reviewed for additional articles. Meta-analyses, systematic reviews, practice guidelines, and randomized clinical trials (RCTs), as well as high-quality articles of greatest interest to general clinicians, were prioritized. Of the 5642 articles identified, 88 were included; consisting of 39 systematic reviews and/or meta-analyses, 13 consensus statements/international guidelines, 12 reviews, 21 cohort studies, and 3 RCTs. Estimates of effect from the included studies were extracted with their 95% CI or 95% credible interval (CrI) for bayesian analyses. Standardized mean differences (SMDs) are interpreted as follows: 0.2 = small effect; 0.5 = medium effect; and 0.8 = large effect. Reductions in pain are indicated by a negative SMD; improvements in function are indicated by a positive SMD.

© 2023 American Medical Association. All rights reserved.

SHOUT
SHARE
IT

Box. Questions and Answers for Clinicians

Are Plain Film Radiographs Necessary for Diagnosing Knee OA?
Plain film radiographs are not required for a diagnosis of knee osteoarthritis (OA), as the diagnosis is primarily based on patient history and physical examination. However, plain film radiographs may be indicated when the presentation is atypical (eg, prolonged joint stiffness, severe pain) to help guide surgical referral, when another diagnosis is strongly suspected (eg, calcium pyrophosphate crystal deposition disease), or when there is an unexpected rapid progression of symptoms (eg, rapidly progressive OA) or change in clinical characteristics (eg, red swollen knee with night pain).

What Are the Indications for Total Knee Replacement in Knee OA?
Total knee replacement is indicated when patients have used all appropriate first- and second-line conservative treatment options and have end-stage OA (eg, no or minimal joint space, persistent pain disrupting sleep, and severe functional loss).

How Effective Is Total Knee Replacement for Relieving Symptoms of Knee OA?
Approximately 80% of patients undergoing total knee replacement report substantial improvement in pain; however, up to one-third report unfavorable outcomes between 3 months and 5 years postoperatively, emphasizing the importance of preoperative patient selection.

When Should a Patient With Acute Knee Pain Be Referred to an Orthopedic Surgeon?
Patients with a history of knee trauma and swelling with an acutely obstructed (locked) knee or unstable knee that gives way should be referred to an orthopedic surgeon. Other specialists (eg, sports medicine physician, physical therapist) may also be appropriate to manage the acutely injured knee and help anticipate the need for orthopedic input (eg, for significant internal or ligamentous derangement, persistent symptoms after 4-6 weeks of exercise therapy).

What Are the First-Line Treatments for Patellofemoral Pain?
First-line treatments for patellofemoral pain include exercises that focus on strengthening the hip and thigh muscles, typically prescribed and supervised by a physical therapist. Shoe orthotics/insoles and patellar taping may be effective adjunctive treatments.

Osteoarthritis

Definition and Pathophysiology

Osteoarthritis is a chronic joint disorder manifesting as the structural and functional failure of synovial joints.[5] Osteoarthritis is no longer considered a cartilage-centric or wear-and-tear disease because it affects the whole joint, with local derangements of articular cartilage and subchondral bone as well as alterations to synovium, menisci, ligaments, and surrounding muscles and fat pads.[6,7] Pain is the primary reason for seeking medical consultation and a major cause of health service utilization.[8]

The pathogenic process of OA is characterized by mechanical, inflammatory, and metabolic factors, leading to an imbalance between the repair and destruction of joint tissues. The pain in early-stage knee OA is typically intermittent, predictable (nociceptive in nature, ie, commensurate in response to tissue damage), and mostly present during weight bearing (mechanical). Nociceptive pain may progress to more constant pain, likely reflecting other neurobiological mechanisms such as sensitization, in which neural pathways become overresponsive to both nociceptive and nonnociceptive stimuli, resulting in increased sensitivity to these stimuli.[9,10]

Epidemiology

Osteoarthritis is the most common joint disease worldwide, with the knee being most frequently affected. A 2020 meta-analysis of 73 studies with 9 440 250 participants estimated a global knee OA prevalence of 23% (95% CI, 20%-26%) in adults older than 40 years (approximately 654 million individuals).[2] The lifetime risk of symptomatic knee OA by age 85 years is 45% (95% CI, 40%-49%).[11] Approximately 61% of adults older than 45 years have radiographic evidence of knee OA, half of whom have knee symptoms.[12]

Risk Factors

The prevalence of knee OA rises with increasing age.[8] In a 2015 meta-analysis including 3446 studies and 415 613 patients, the main risk factors associated with knee OA were female sex (11 studies; pooled odds ratio [OR], 1.68; 95% CI, 1.37-2.07), obesity (22 studies; pooled OR, 2.66; 95% CI, 2.15-3.28), and previous knee injury (13 studies; pooled OR, 2.83; 95% CI, 1.91-4.19) (absolute rates were not reported).[13] Population-attributable fractions calculated from a prospective cohort study conducted as phase 2 in the same article (n = 3907) showed that 25% and 5% of new knee OA cases could be attributed to being overweight and having a previous knee injury, respectively.[13] Other risk factors include occupations with repetitive joint use such as squatting and kneeling (eg, farming),[14] knee malalignment,[15] and quadriceps muscle weakness.[16] Knee OA accounts for approximately 85% of the global disability burden of OA.[17]

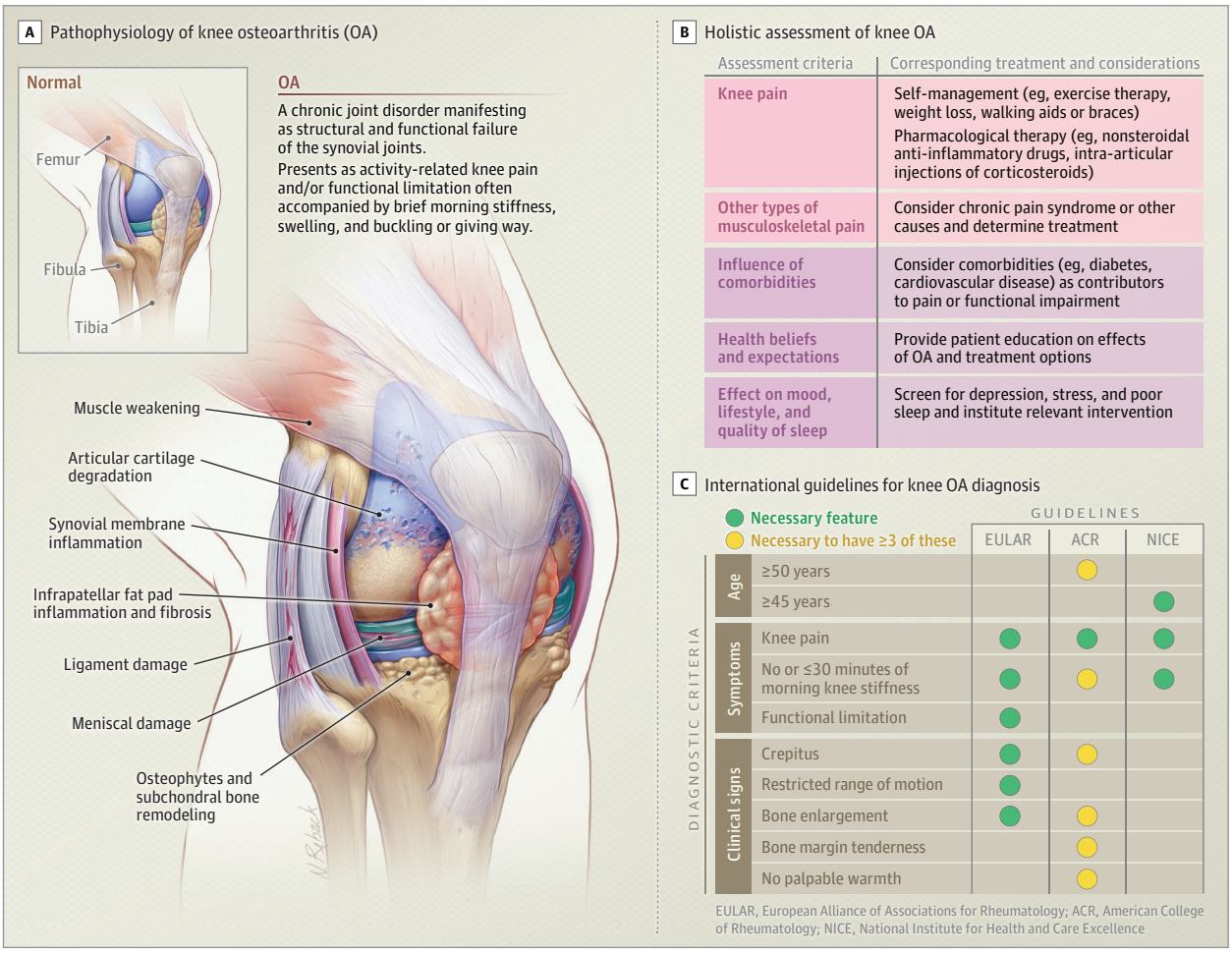
Clinical Presentation and Diagnosis

The most frequent symptoms of knee OA are activity-related knee pain (95% sensitivity; 19% specificity) and/or functional limitations (56% sensitivity; 63% specificity), usually accompanied by brief (<30 minutes) morning stiffness (88% sensitivity; 52% specificity), swelling (43% sensitivity; 41% specificity), and buckling or giving way (26% sensitivity; 79% specificity).[18] Symptoms usually start gradually during a prolonged history of discomfort interspersed with self-limited flare-ups.[19] The cardinal signs of knee OA on physical examination include crepitus (89% sensitivity; 60% specificity), bony enlargement (55% sensitivity; 95% specificity), and restricted range of motion (17% sensitivity; 96% specificity).[20]

According to the 2022 National Institute for Health and Care Excellence (NICE) guideline from the United Kingdom, OA can be diagnosed clinically without imaging in patients aged 45 years or older presenting with activity-related joint pain with no or less than 30 minutes of morning stiffness (**Figure 1**).[21] As part of a holistic clinical assessment (Figure 1), it is important to inquire about the impact of knee pain on function (80% of patients with OA have movement limitation; 25% cannot perform major activities of daily living).[8] Laboratory tests or radiographs are indicated only when the presentation is atypical (eg, prolonged joint stiffness, resting

© 2023 American Medical Association. All rights reserved.

Figure 1. Overview of Knee Osteoarthritis Pathophysiology, Assessment, and Diagnosis


A Pathophysiology of knee osteoarthritis (OA)
Normal
Femur
Fibula
Tibia
OA
A chronic joint disorder manifesting as structural and functional failure of the synovial joints.
Presents as activity-related knee pain and/or functional limitation often accompanied by brief morning stiffness, swelling, and buckling or giving way.
Muscle weakening
Articular cartilage degradation
Synovial membrane inflammation
Infrapatellar fat pad inflammation and fibrosis
Ligament damage
Meniscal damage
Osteophytes and subchondral bone remodeling
B Holistic assessment of knee OA
Assessment criteria
Corresponding treatment and considerations
Knee pain
Self-management (eg, exercise therapy, weight loss, walking aids or braces)
Pharmacological therapy (eg, nonsteroidal anti-inflammatory drugs, intra-articular injections of corticosteroids)
Other types of musculoskeletal pain
Consider chronic pain syndrome or other causes and determine treatment
Influence of comorbidities
Consider comorbidities (eg, diabetes, cardiovascular disease) as contributors to pain or functional impairment
Health beliefs and expectations
Provide patient education on effects of OA and treatment options
Effect on mood, lifestyle, and quality of sleep
Screen for depression, stress, and poor sleep and institute relevant intervention
C International guidelines for knee OA diagnosis
Necessary feature
Necessary to have ≥3 of these
GUIDELINES
EULAR
ACR
NICE
DIAGNOSTIC CRITERIA
Age
≥50 years
≥45 years
Symptoms
Knee pain
No or ≤30 minutes of morning knee stiffness
Functional limitation
Clinical signs
Crepitus
Restricted range of motion
Bone enlargement
Bone margin tenderness
No palpable warmth
EULAR, European Alliance of Associations for Rheumatology; ACR, American College of Rheumatology; NICE, National Institute for Health and Care Excellence

pain), when another diagnosis is strongly suspected (eg, calcium pyrophosphate crystal deposition disease), or when there is unexpected rapid progression of symptoms (eg, rapidly progressive OA) or change in clinical characteristics (eg, red, swollen knee with night pain).[22] Although plain film radiographs are not recommended for diagnosing knee OA, they may be helpful to document stage of OA severity, predict prognosis, and ascertain the likely response to surgical treatment (ie, guide referral to an orthopedic surgeon).[23]

Referral, Treatment, and Outcomes

Current treatment approaches are focused on relieving symptoms,[24] as no treatment has been identified for disease modification (eg, improvements in both symptoms and joint structure, such as cartilage health).[25] First-line symptomatic management comprises nonpharmacological approaches including (1) exercise therapy; (2) weight loss (if overweight or obese); (3) prescription of walking aids or braces (if indicated, eg, during pain flares); and (4) education and self-management, alongside possible institution of pharmacological options such as nonsteroidal anti-inflammatory drugs (NSAIDs; topical or oral) and, only if required (ie, inadequate response to all other therapies), intra-articular therapies such as steroids. The indication for surgical interventions is typically end-stage knee OA (defined as no or minimal joint space with inability to cope with pain) after conservative options have not effectively relieved symptoms.[21,24,26,27] The effects of interventions on pain and function are provided in **Table 1**, and strength of recommendations from the latest treatment guidelines are shown in **Figure 2**.

In a 2021 meta-analysis, patient education alone (ie, any form of therapist-facilitated education) compared with no education intervention was associated with less knee pain (6 trials; SMD, −0.35; 95% CI, −0.56 to −0.14) and improved physical function, although this outcome did not reach statistical significance (6 trials; SMD, 0.31; 95% CI, 0.00-0.62).[28] Individually supervised exercises provided greater pain reduction (23 studies; SMD, −0.61; 95% CI, −0.43 to −0.80) than group-based exercises (19 studies; SMD, −0.37; 95% CI, −0.20 to −0.54).[38] In a meta-analysis of 3 studies, a soft knee brace that augmented exercise therapy compared with no knee brace showed a reduction in pain (SMD, −0.61; 95% CI, −0.89 to −0.33) and improved function (SMD, 0.39; 95% CI, 0.11-0.67).[31] In mild to moderate knee OA (ie, radiographic joint space width loss), 5% to 10% weight loss was associated with less pain (5 trials; SMD, −0.33; 95% CI, −0.17 to −0.48) and improved function (5 trials; SMD, 0.42; 95% CI, 0.25-0.59).[30]

In a 2020 network meta-analysis with 122 RCTs and 47 113 participants, topical NSAIDs compared with acetaminophen were associated with improved function (SMD, 0.29; 95% CrI,

© 2023 American Medical Association. All rights reserved.

Table 1. Effectiveness of Recommended Interventions on Pain and Function in Knee Osteoarthritis From Meta-Analyses

Type of intervention	Follow-up duration	Standardized mean difference (95% CI)[a]		Level of evidence[c]
		Pain[b]	Function[b]	
Nonpharmacological				
Patient education vs usual care[28]				
	<6 mo	−0.35 (−0.56 to −0.14) favoring education; 6 trials	0.31 (0.00-0.62) favoring education; 6 trials[d]	Low
	6-12 mo	−0.10 (−0.26 to 0.05) favoring education; 4 trials[d]	0.17 (−0.07 to 0.40) favoring education; 4 trials[d]	Low
	≥12 mo	−0.12 (−0.30 to 0.05) favoring education; 2 trials[d]	Not reported	Low
Patient education plus exercise vs patient education alone[28]				
	<6 mo	−0.44 (−0.19 to −0.69) favoring education plus exercise; 5 trials	0.81 (0.54-1.08) favoring education plus exercise; 3 trials	Low
	6-12 mo	−0.14 (−0.32 to 0.04) favoring education plus exercise; 4 trials[d]	0.39 (0.15-0.62) favoring education plus exercise; 2 trials	Low
	≥12 mo	−0.17 (−0.33 to 0.13) favoring education plus exercise; 2 trials[d]	0.24 (−0.06 to 0.54) favoring education plus exercise; 2 trials[d]	Low
Land-based exercise vs nonexercise control[29]				
	Immediate posttreatment	−0.49 (−0.59 to −0.39) favoring exercise; 44 trials	0.52 (0.39-0.64) favoring exercise; 44 trials	Moderate to high
	2-6 mo posttreatment	−0.24 (−0.35 to −0.14) favoring exercise; 12 trials	0.15 (0.04-0.26) favoring exercise; 10 trials	Moderate to high
Weight loss diet vs control/exercise[30]	Not reported	−0.33 (−0.17 to −0.48) favoring weight loss; 4 trials	0.42 (0.25-0.59) favoring weight loss; 4 trials	Not reported
Knee braces vs usual care[31]	>6 wk	−0.61 (−0.33 to −0.89) favoring knee braces; 3 trials	0.39 (0.11-0.67) favoring knee brace; 3 trials	Low
Nonsteroidal anti-inflammatory drugs (NSAIDs)				
Acetaminophen (paracetamol) vs placebo[32]	3-12 wk	−0.32 (−0.54 to −0.10) favoring acetaminophen; 7 trials[e]	0.29 (0.10-0.49) favoring acetaminophen; 7 trials[e]	High
Topical NSAIDs vs acetaminophen[33]				
	4 wk	−0.09 (95% CrI, −0.55 to 0.37) favoring topical NSAIDs; 66 trials[d]	0.29 (95% CrI, 0.06-0.52) favoring topical NSAIDs; 52 trials	Not reported
	12 wk	−0.20 (95% CrI, −1.07 to 0.64) favoring topical NSAIDs; 16 trials[d]	0.24 (95% CrI, −0.29 to 0.79) favoring topical NSAIDs; 16 trials[d]	Not reported
Topical NSAIDs vs oral NSAIDs[33]				
	4 wk	−0.21 (95% CrI, −0.58 to 0.16) favoring oral NSAIDs; 66 trials[d]	0.03 (95% CrI, −0.16 to 0.22) favoring oral NSAIDs; 52 trials[d]	Not reported
	12 wk	−0.05 (95% CrI, −0.55 to 0.44) favoring topical NSAIDs; 16 trials[d]	0.03 (95% CrI, −0.33 to 0.37) favoring oral NSAIDs; 16 trials[d]	Not reported
Oral NSAIDs vs placebo[34]				
	2 wk	−0.40 (−0.46 to −0.35) favoring oral NSAIDs; 32 trials	0.44 (0.37-0.50) favoring oral NSAIDs; 15 trials	Not reported
	26 wk	−0.21 (−0.39 to −0.03) favoring oral NSAIDs; 2 trials	0.19 (0.07-0.32) favoring oral NSAIDs; 2 trials	Not reported
Intra-articular injections				
Corticosteroid vs placebo[35]				
	≤6 wk	−1.51 (−1.80 to −1.20) favoring corticosteroid; 2 trials	1.78 (0.23-3.32) favoring corticosteroid; 2 trials	Not reported
	>6 wk and <24 wk	−0.72 (−1.96 to 0.53) favoring corticosteroid; 2 trials[d]	0.70 (0.62-0.98) favoring corticosteroid; 2 trials	Not reported
Hyaluronic acid vs placebo[36]				
Single injection	3 mo	−0.03 (−0.29 to 0.23) favoring hyaluronic acid; 1 trial[d]	Not reported	Not reported
	6 mo	−0.04 (−0.20 to 0.13) favoring hyaluronic acid; 2 trials[d]	Not reported	Not reported
2-4 Injections	3 mo	−0.76 (−0.98 to −0.53) favoring hyaluronic acid; 6 trials[d]	Not reported	Not reported
	6 mo	−0.36 (−0.63 to −0.09) favoring hyaluronic acid; 11 trials	Not reported	Not reported
≥5 Injections	3 mo	−0.20 (−0.43 to 0.03) favoring hyaluronic acid; 3 trials[d]	Not reported	Not reported
	6 mo	−0.18 (−0.35 to −0.01) favoring hyaluronic acid; 8 trials	Not reported	Not reported

(continued)

© 2023 American Medical Association. All rights reserved.

Table 1. Effectiveness of Recommended Interventions on Pain and Function in Knee Osteoarthritis From Meta-Analyses (continued)

Type of intervention	Follow-up duration	Standardized mean difference (95% CI)[a]		Level of evidence[c]
		Pain[b]	Function[b]	
Surgery				
Total knee replacement (no comparator, cohort studies only)[37]				
	Baseline	64.0 (60.2-67.7); 58 trials[f]	47.1 (45.7-48.4); 146 trials[g]	Not reported
	3 mo	24.1 (20.3-27.9)[f]	72.8 (71.3-74.4)[g]	Not reported
	6 mo	20.4 (16.7-24.0)[f]	76.3 (74.7-77.8)[g]	Not reported
	1 y	16.9 (13.6-20.3)[f]	78.1 (76.4-79.7)[g]	Not reported
	5 y	11.1 (7.9-14.3)[f]	Not reported	Not reported
	10 y	10.1 (4.8-15.4)[f]	79.7 (77.9-81.5)[g]	Not reported

Abbreviation: CrI, credible interval.

[a] Standardized mean difference is interpreted as 0.2 = small effect; 0.5 = medium effect; and 0.8 = large effect.

[b] For the outcome of pain, a negative standardized mean difference indicates less pain following the intervention. For the outcome of function, a positive standardized mean difference indicates improved function following the intervention.

[c] Level of evidence assessed using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) or specific criteria by the individual meta-analysis.

[d] This outcome did not reach statistical significance.

[e] Values are mean difference (95% CI) on a 0- to 10-point scale.

[f] Values are mean (95% CI) pain scores (0 = no pain; 100 = worst pain).

[g] Values are mean (95% CI) function scores (0 = worst function; 100 = best function).

0.06-0.52), but the pain response was similar (SMD, −0.09; 95% CrI, −0.55 to 0.37). Topical NSAIDs had a better safety profile (eg, gastrointestinal adverse events: risk ratio, 0.52; 95% CrI, 0.35-0.76).[33] In a 2020 meta-analysis of placebo-controlled RCTs, oral NSAIDs were associated with less pain (32 trials, 12875 patients; SMD, −0.40; 95% CI, −0.46 to −0.35) and improved function (15 trials, 5619 patients; SMD, 0.44; 95% CI, 0.37-0.50) at 2 weeks, with attenuating effects over 26 weeks.[34] Traditional NSAIDs produced the largest improvements in pain: 24% and 64% greater improvement than celecoxib and intermediate cyclooxygenase inhibitors (eg, meloxicam), respectively, at 2 weeks, and 33% and 44%, respectively, at 12 weeks. NSAID risk should be mitigated by regular monitoring for adverse reactions, minimizing dose and keeping treatment duration brief, as suggested by the 2019 American College of Rheumatology (ACR) guidelines. According to the guidance provided in the ACR guidelines, on the basis of toxicity and limited efficacy, commonly used therapies, including acetaminophen, duloxetine, and tramadol, are only conditionally recommended.[26]

As described in Figure 2, the 2019 ACR and 2022 NICE guidelines recommend intra-articular steroids for short-term efficacy (moderate-quality evidence) but recommend against intra-articular hyaluronic acid (low-quality evidence) as second-line treatment. In a 2021 meta-analysis, intra-articular steroids resulted in less pain (2 trials; SMD, −1.51; 95% CI, −1.80 to −1.20) and improved function (2 trials; SMD, 1.78; 95% CI, 0.23-3.32) for up to 6 weeks compared with intra-articular saline; no serious adverse events were reported.[39] A recent review of the efficacy and safety profiles of different intra-articular therapies (steroids, hyaluronic acid, platelet-rich plasma, stem cells, and prolotherapy [intra-articular injection of an irritant solution such as hyperosmolar dextrose]) reported uncertain long-term effectiveness of these therapies due to lack of long-term data and methodological flaws despite reporting short-term benefits in knee OA.[35]

Surgical referral for total knee replacement can be considered for patients with advanced stages of structural (plain film radiographic changes) and symptomatic OA despite using (for >6 months) all appropriate first- and second-line conservative options discussed above.[5] In this setting, plain film radiographs are helpful to guide referral. An improvement in pain following total knee replacement is not guaranteed. Poor outcome (long-term pain at 3 months to 5 years after total knee replacement) is reported in 10% to 34% of patients,[40,41] highlighting the importance of careful preoperative patient selection. A 2021 meta-analysis (58 studies, 16 164 patients) reported marked improvement (47 points on a 0- to 100-point scale) in pain in the first 12 months after total knee replacement, but some pain and functional limitation typically persist in the long term[37] (Table 1).

There is substantial evidence to suggest that many other commonly used treatments, including supplements (eg, glucosamine, chondroitin), acetaminophen, opioids, acupuncture, and arthroscopy have no clinically meaningful benefit over placebo.[21,24,26] An overview of diagnosis and treatment of knee OA, as well as PFP and meniscal tears, is provided in **Table 2**.

Patellofemoral Pain

Definition and Pathophysiology

Patellofemoral pain refers to pain behind or around the patella, also known as runner's knee or chondromalacia patella.

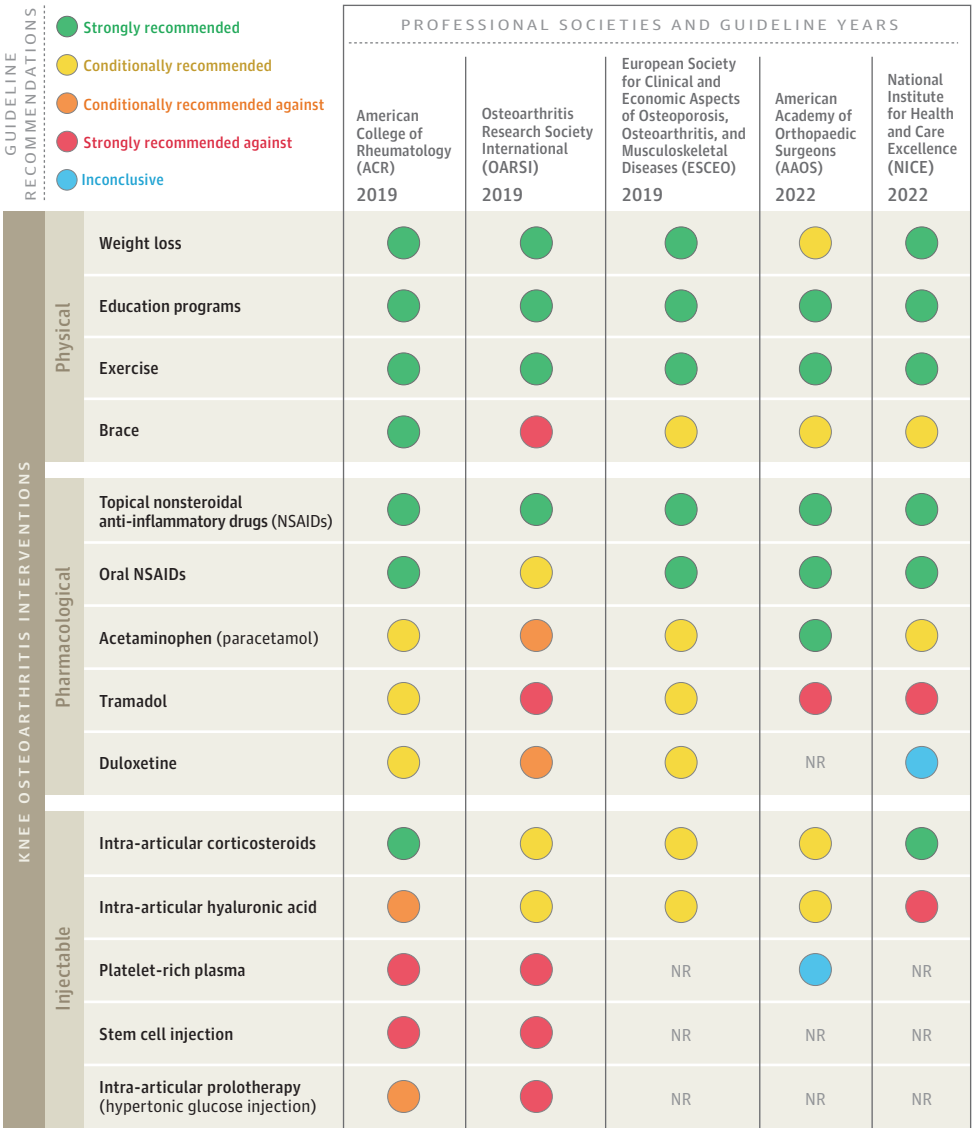
The exact pathogenesis of PFP remains unclear but is likely multifactorial. Proposed mechanisms include abnormal loading of the patellofemoral joint[50] due to a combination of patellar maltracking or muscle imbalance[51] or increased patella intraosseous pressure.[52]

Epidemiology

Patellofemoral pain accounts for 11% to 17% of all knee pain in patients in general practice.[53] The condition typically affects active people younger than 40 years (**Figure 3**). Patellofemoral pain was once considered a self-limiting condition; however, symptoms can persist for years.[54] A systematic review of 23 studies (n = 6102 patients

© 2023 American Medical Association. All rights reserved.

Figure 2. Summary of Knee Osteoarthritis Treatment Guidelines From Major Professional Societies



NR indicates not reported in the guidelines. The recommendations by different professional societies are heterogeneous regarding most pharmacological interventions, depending on the methodologies used for guideline development.

contributing to prevalence data) estimated that the prevalence of PFP in the general population was 22.7%, and 28.9% in adolescents.[3]

Risk Factors

In a 2019 meta-analysis,[55] lower absolute quadriceps strength was a risk factor for PFP, especially when adjusted for body mass index (2 studies, 158 participants; SMD, −0.69; 95% CI, −1.02 to −0.35; favoring higher quadriceps strength as protective).[55] Greater hip abduction strength was a risk factor for PFP in adolescents (2 studies, 342 participants; SMD, 0.71; 95% CI, 0.39-1.04; favoring lower hip abduction strength as protective).[55]

Clinical Presentation and Diagnosis

Patellofemoral pain presents with gradual-onset generalized anterior knee pain, aggravated by loading a flexed knee (eg, climbing stairs).[53] Pain is rarely present when the patellofemoral joint is unloaded (eg, sitting).[56]

There is no definitive clinical test to diagnose PFP[42]; it is a diagnosis of exclusion after ruling out other intra-articular and peripatellar pathology. Differential diagnoses for PFP include patellar tendinopathy, patellar subluxation, Osgood-Schlatter disease, or systemic rheumatic diseases. A 2013 systematic review found that anterior knee pain during a squat was the most sensitive test to diagnose PFP (Figure 3) (91% sensitivity [95% CI, 79%-96%]; 50% specificity [95% CI, 31%-69%]).[42]

Imaging, such as radiographs or ultrasound, is not required to diagnose PFP initially but may help identify alternative causes of pain (eg, magnetic resonance imaging [MRI] for osteochondral lesion, ultrasound for tendinopathy) only when there is no response to treatment.[57] Ultrasound is both sensitive (85%) and specific (100%)

© 2023 American Medical Association. All rights reserved.

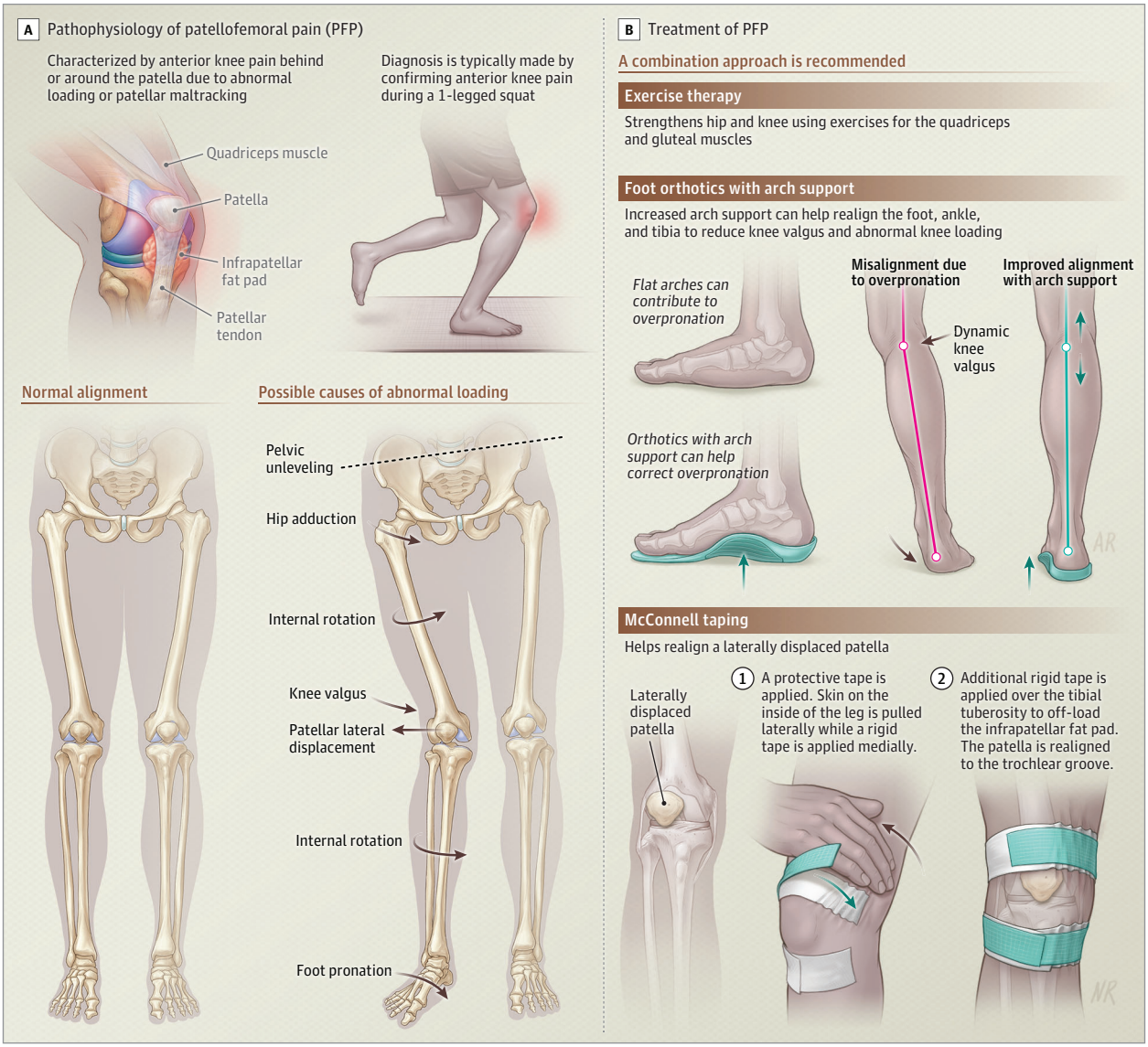
Table 2. Diagnosis and Treatment of Common Knee Conditions

	Osteoarthritis (OA)	Patellofemoral pain	Meniscal tears
Presenting symptoms	Insidious-onset use-related knee pain and/or functional limitations (mostly in older adults): brief morning stiffness, crepitus, swelling, reduced range of motion, joint instability, bony enlargement, muscle weakness, fatigue	Insidious-onset generalized anterior knee pain around or behind the patella, typically in younger adults, which is aggravated by loading a flexed knee	• Pain localized to the knee joint line and accompanying effusion • Traumatic tear: acute onset often following twisting injury in individuals aged <40 y • Degenerative tear: insidious onset in adults aged ≥40 y
Diagnostic evaluation	Diagnosis of knee OA can be made when patients aged >45 y present with activity-related knee joint pain and no or brief (<30 min) early morning stiffness (95% sensitivity, 69% specificity)[18]	Clinical examination: presence of anterior knee pain during a single-leg squat is the best clinical test (91% sensitivity, 50% specificity)[42]	• Provocation of symptoms on a combination of clinical tests (McMurray test, joint line tenderness): positive likelihood ratio, 2.7 (95% CI, 1.4-5.1); negative likelihood ratio, 0.4 (95% CI, 0.2-0.7)[43] • McMurray test: 61% sensitivity, 84% specificity[44]; joint line tenderness: 83% sensitivity, 83% specificity[44]; magnetic resonance imaging[45]: 78%-89% sensitivity, 88%-95% specificity
First-line therapy	Weight loss, exercise therapy, and health education	Physical therapy: hip and knee exercises in combination with foot orthotics and patellar taping	• Physical therapy to strengthen knee muscles, return to activity • Traumatic bucket-handle tears and those concomitant with ACL rupture may require surgery
Efficacy of first-line therapy	• A 5%-10% weight loss significantly lowers pain (SMD, −0.33; 95% CI, −0.48 to −0.17) and improves function (SMD, 0.42; 95% CI, 0.25-0.59)[30] • Exercise therapy combined with patient education provides clinically significant reductions in pain (SMD, −0.44; 95% CI, −0.69 to −0.19) and improvements in function (SMD, 0.81; 95% CI, 0.54-1.08) at 6 mo[28]	Exercise therapy reduces pain (SMD, −1.46; 95%CI, −2.39 to −0.54) and improves function (SMD, 1.10; 95% CI, 0.58-1.63) vs control (no treatment, placebo, or wait-list) at 3 mo[46]	• Traumatic tears: 12 wk of exercise therapy associated with similar reductions in pain to surgery (partial meniscectomy/repair) (121 patients; mean difference at 12-mo follow-up, 5.4 [95% CI, −0.7 to 11.4] out of 100)[47] • Degenerative tears: partial meniscectomy provides no benefit over placebo surgery (146 patients; SMD at 12-mo follow-up, −0.08 [95% CI, −0.41 to 0.24] favoring placebo)[48]
Adverse events of first-line therapy	No serious adverse events from exercise therapy	• No serious adverse events from exercise therapy; foot orthotics can cause local blisters, foot discomfort • Taping can cause a local skin reaction • Delayed diagnosis can lead to delayed recovery, development of patellofemoral OA	• Exercise therapy: worsening of tear • Surgery (events per 1000 cases)[49]: deep vein thrombosis, 4.1 (95% CI, 1.8-9.6); pulmonary embolism, 1.5 (95% CI, 0.6-3.5); venous thromboembolism, 5.7 (95% CI, 3.0-10.9); infection, 2.1 (95% CI, 0.8-5.6); death, 1.0 (95% CI, 0.0-23.9)
Surgical options	Knee replacement for end-stage OA with persistent pain and severe function loss	Not recommended for patellofemoral pain	Arthroscopic partial meniscectomy or meniscal repair for certain limited indications (eg, displaced bucket-handle tear, concomitant with ACL reconstruction, after 3 mo of exercise therapy)

Abbreviations: ACL, anterior cruciate ligament; SMD, standardized mean difference.

© 2023 American Medical Association. All rights reserved.

Figure 3. Overview of Patellofemoral Pain Pathophysiology, Assessment, and Treatment


A Pathophysiology of patellofemoral pain (PFP)
Characterized by anterior knee pain behind or around the patella due to abnormal loading or patellar maltracking
Diagnosis is typically made by confirming anterior knee pain during a 1-legged squat
Quadriceps muscle
Patella
Infrapatellar fat pad
Patellar tendon
Normal alignment
Possible causes of abnormal loading
Pelvic unleveling
Hip adduction
Internal rotation
Knee valgus
Patellar lateral displacement
Internal rotation
Foot pronation
B Treatment of PFP
A combination approach is recommended
Exercise therapy
Strengthens hip and knee using exercises for the quadriceps and gluteal muscles
Foot orthotics with arch support
Increased arch support can help realign the foot, ankle, and tibia to reduce knee valgus and abnormal knee loading
Flat arches can contribute to overpronation
Misalignment due to overpronation
Dynamic knee valgus
Improved alignment with arch support
Orthotics with arch support can help correct overpronation
McConnell taping
Helps realign a laterally displaced patella
Laterally displaced patella
1 A protective tape is applied. Skin on the inside of the leg is pulled laterally while a rigid tape is applied medially.
2 Additional rigid tape is applied over the tibial tuberosity to off-load the infrapatellar fat pad. The patella is realigned to the trochlear groove.

for PFP when MRI is not available or contraindicated.[57] In the presence of radiographic changes in the patellofemoral joint, PFP can be a presenting symptom of patellofemoral OA.[58]

Referral, Treatment, and Outcomes

Patients with PFP should be referred to a physical therapist and/or podiatrist. The latest (2018) consensus statement on PFP, informed by systematic review and RCT evidence, recommends supervised hip and knee exercises in combination with foot orthoses[59] or patellar taping[60] as first-line treatment.[61]

In a 2015 meta-analysis, short-term therapeutic exercise (≤3 months) compared with control interventions was associated with less activity-related pain (5 trials, 375 patients; mean difference, −1.46; 95% CI, −2.39 to −0.54 [on a 0- to 10-point scale]) and improved function (7 trials, 483 patients; SMD, 1.10; 95% CI, 0.58-1.63).[46]

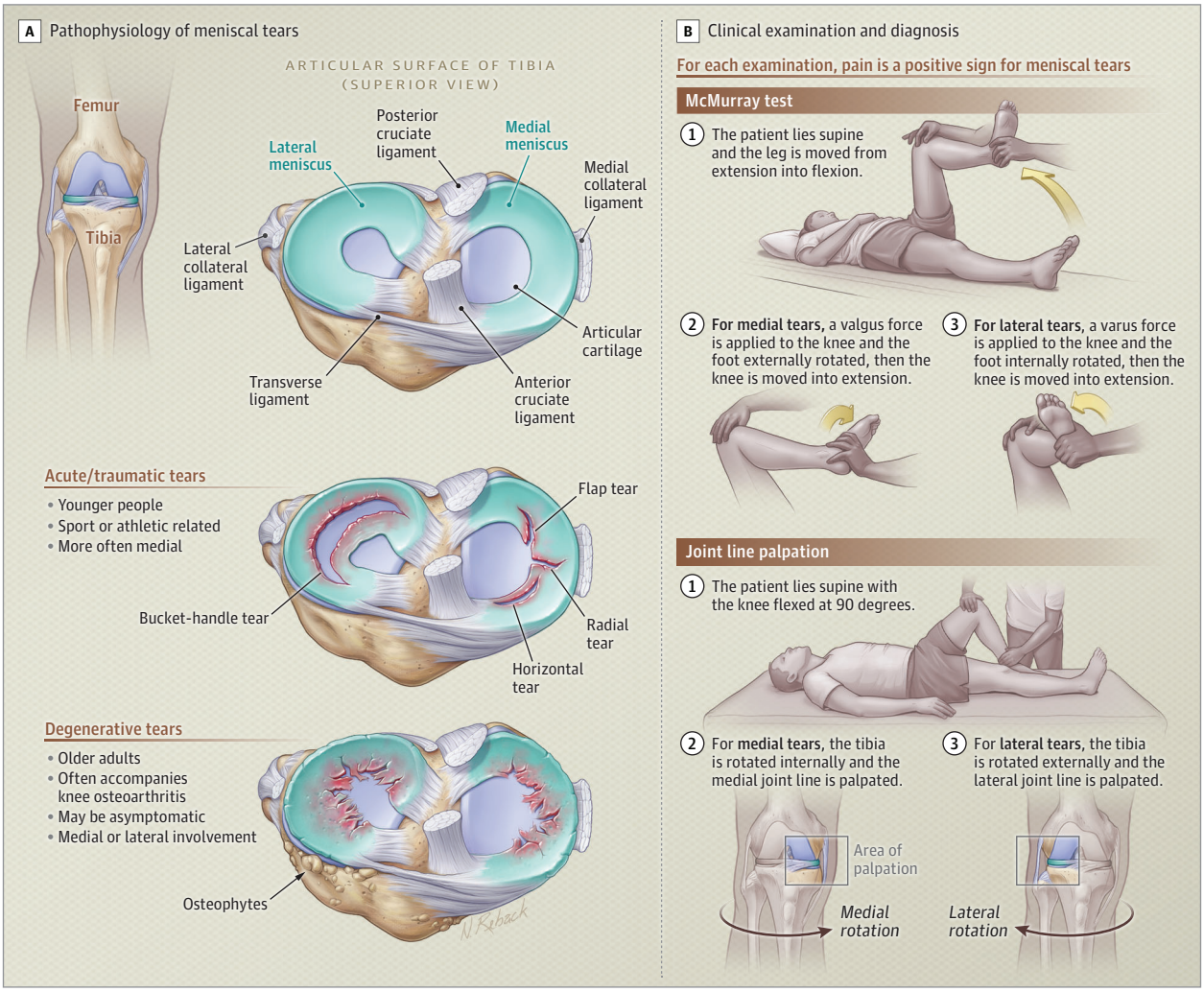
An RCT of 179 participants comparing off-the-shelf foot orthoses with an inbuilt arch support to flat inserts demonstrated less pain in the short term (≤6 weeks) (visual analog scale: 0 = no pain; 100 = worst pain) for the foot orthoses group, but the confidence interval was broad, suggesting inconsistent treatment response for participants (mean difference, −8.0; 99% CI, −18.1 to 2.1).[59]

There are various taping techniques used for PFP. The most common is the McConnell technique (rigid tape repositions the patella within the femoral trochlea), typically performed by physical therapists. A 2017 systematic review conducted on McConnell and kinesiotaping techniques for PFP found that taping was associated with improved outcomes, defined as improved pain when combined with exercise, but taping in isolation was not associated with improved outcomes.[60]

There is limited evidence for acupuncture and running retraining (training to change foot-strike patterns). A systematic review comprising 20 studies (945 participants) on medical interventions for PFP (eg, NSAIDs) or nutraceuticals (eg, glucosamine) found low quality of evidence to support these treatments.[62] Injections, such as hyaluronic acid, have shown no clinically meaningful differences

© 2023 American Medical Association. All rights reserved.

Figure 4. Overview of Meniscal Tear Pathophysiology, Clinical Examination, and Diagnosis


A Pathophysiology of meniscal tears
ARTICULAR SURFACE OF TIBIA (SUPERIOR VIEW)
Femur
Tibia
Posterior cruciate ligament
Medial meniscus
Lateral meniscus
Medial collateral ligament
Lateral collateral ligament
Articular cartilage
Transverse ligament
Anterior cruciate ligament
Acute/traumatic tears
• Younger people
• Sport or athletic related
• More often medial
Flap tear
Bucket-handle tear
Radial tear
Horizontal tear
Degenerative tears
• Older adults
• Often accompanies knee osteoarthritis
• May be asymptomatic
• Medial or lateral involvement
Osteophytes
B Clinical examination and diagnosis
For each examination, pain is a positive sign for meniscal tears
McMurray test
1 The patient lies supine and the leg is moved from extension into flexion.
2 For medial tears, a valgus force is applied to the knee and the foot externally rotated, then the knee is moved into extension.
3 For lateral tears, a varus force is applied to the knee and the foot internally rotated, then the knee is moved into extension.
Joint line palpation
1 The patient lies supine with the knee flexed at 90 degrees.
2 For medial tears, the tibia is rotated internally and the medial joint line is palpated.
3 For lateral tears, the tibia is rotated externally and the lateral joint line is palpated.
Area of palpation
Medial rotation
Lateral rotation

in pain at 6-month follow-up, but worse function (SMD, −0.5; 95% CI, −1.0 to −0.1).[62] Platelet-rich plasma reduced pain, favoring 3 injections over 1 (SMD, −1.1; 95% CI, −2.0 to −0.3), but this evidence was of low certainty due to inadequate blinding and randomization of participants and the absence of a control group.[62] Referral for surgery (eg, arthroscopy to remove damaged structures, patellofemoral arthroplasty) is generally not indicated for PFP given the lack of RCT evidence on the benefit of surgery.[56]

Patellofemoral pain is on a continuum with patellofemoral OA—up to 69% of patients with chronic PFP exhibit radiographic changes of the patellofemoral joint.[63] Individuals with PFP exhibit similar signs and symptoms to those with patellofemoral OA (eg, knee malalignment, quadriceps weakness) and therefore share similar treatment targets.

Although PFP was formerly thought of as a self-limiting condition, a 2016 multicenter observational analysis combining data from 2 RCTs (n = 179 and n = 131) found that 57% of participants with PFP reported unfavorable recovery (perceived global recovery Likert scale) at 5 to 8 years after recruitment, with mean pain scores rated as 29.9 (SD, 27.7) on a 0- to 100-point visual analog scale.[54] More resting pain and activity-related pain predicted worse prognosis 1 year posttreatment, irrespective of intervention.[64]

Meniscal Tears

Definition and Pathophysiology

The meniscus is a fibrocartilaginous structure within the knee joint, consisting of 2 (medial and lateral) semicircular components that transfer load and aid joint stability.[65] Meniscal tears (ie, separation of fibrous structure) can be classified as traumatic (resulting from excessive shear force) or degenerative (resulting from repetitive forces on a deteriorated meniscus). Tears can also be defined based on pattern and location, which can influence healing (**Figure 4**).

Epidemiology

According to a Swedish population-wide report from 2014, the annual incidence of clinically diagnosed meniscal tears was 79 (95% CI, 63-94) per 100 000 persons.[66] Acute traumatic tears are most prevalent in active young populations (aged 18-40 years)

© 2023 American Medical Association. All rights reserved.

who engage in sports and often accompany cruciate ligament injuries.[67]

Degenerative tears, typically affecting older adults (aged ≥40 years), are commonly found in patients with knee OA. In a US population-based study of 991 randomly selected adults, 63% of older adults with symptomatic OA had an MRI-diagnosed meniscal tear.[68] However, incidental meniscal tears on imaging are also common. A meta-analysis of 21 studies (2776 adults) showed that 19% (95% CI, 13%-26%) of adults aged 40 years or older without knee pain or injury history had an asymptomatic meniscal tear on MRI.[69]

Risk Factors

A meta-analysis (2 studies, 937 participants) reported that playing pivoting sports, such as soccer (36% vs 16% for nonparticipation; OR, 3.58; 95% CI, 1.87-6.86) and rugby (7% vs 4%; OR, 2.84; 95% CI, 1.48-5.45), but not running (9% vs 7%; OR, 1.24; 95% CI, 0.74-2.07), were associated with a higher prevalence of traumatic meniscal tears compared with not engaging in sports.[70] Meta-analysis also found that the following factors were associated with a higher prevalence of symptomatic degenerative meniscal tears: age older than 60 years (2 studies, 1132 participants; 46% vs 31%; OR, 2.32; 95% CI, 1.80-3.01), male sex (3 studies, 3197 participants; 39% vs 27%; OR, 2.98; 95% CI, 2.30-3.85), work-related kneeling and squatting (3 studies, 1078 participants; 68% vs 38%; OR, 2.69; 95% CI, 1.64-4.40), walking more than 2 miles per day (2 studies, 937 participants; 61% vs 43%; OR, 1.65; 95% CI, 1.22-2.24), lifting or carrying more than 10 kg at least 10 times per week (2 studies, 937 participants; 58% vs 40%; OR, 1.89; 95% CI, 1.41-2.55) and climbing more than 30 stairs per day (2 studies, 937 participants; 45% vs 23%; OR, 2.28; 95% CI, 1.56-3.31).[70] No data were found on running as a risk factor for degenerative meniscal tears.

Clinical Presentation and Diagnosis

Meniscal tears typically present with knee pain localized to the joint line and an accompanying effusion: acute onset, often following a noncontact twisting/rotatory injury for traumatic tears, or insidious onset for degenerative tears. A review of 38 studies identified that mechanical symptoms (ie, knee clicking, catching, locking) have modest sensitivity (0.32-0.69), specificity (0.45-0.74), and positive predictive value (0.75-0.81) for meniscal tear.[71]

Clinical tests help diagnose a meniscal tear by provocation of symptoms (Figure 4) (see **Video**). These include (from a meta-analysis of 9 studies, 1234 participants) McMurray test (61% sensitivity [95% CI, 45%-74%] and 84% specificity [95% CI, 69%-92%]) and joint line tenderness (83% sensitivity [95% CI, 73%-90%] and 83% specificity [95% CI, 61%-94%]).[44] A meta-analysis of 5 studies (594 participants) suggested that a combination of clinical tests (including McMurray and joint line tenderness) is better than individual findings (positive likelihood ratio, 2.7 [95% CI, 1.4-5.1]; negative likelihood ratio, 0.4 [95% CI, 0.2-0.7]).[43]

Systematic use of MRI is not indicated in first-line assessment of meniscal tears, particularly in middle-aged and older adults,[72] in whom asymptomatic meniscal tears are common.[69] Magnetic resonance imaging may be reserved for more complicated cases (eg, persistent symptoms without clear diagnosis) or symptoms (eg, unexplained weight loss, night sweats) concerning for malignancy (eg, bone tumor).[73] If a traumatic meniscal tear cannot be confirmed clinically by an orthopedist, an MRI can specify the type of tear, evaluate cruciate and collateral ligaments, and assist orthopedists as part of their preoperative planning.[74] A meta-analysis (19 studies, 1286 participants) evaluating the diagnostic accuracy of MRI compared with arthroscopy reported 78% to 89% sensitivity and 88% to 95% specificity.[45]

Referral, Treatment, and Outcomes

Patients with a meniscal tear may undergo surgery to remove or repair the torn meniscus or nonsurgical rehabilitation to address impairments associated with the meniscal tear. There is no evidence that surgical management is superior to rehabilitation-based approaches for most traumatic and degenerative meniscal tears. Evidence-based clinical guidelines recommend most patients with a symptomatic meniscal tear be referred to a physical therapist for 3 months or longer of rehabilitation-based care as first-line treatment.[75]

For traumatic meniscal tears, RICE (rest, ice, compression, elevation) has been central to acute management despite a paucity of high-quality evidence.[76] For longer-term outcomes, both surgical and nonsurgical treatments are effective. Two RCTs of 121[47] and 100[77] young adults (mean age, 30-35 years) compared early surgery (arthroscopic partial meniscectomy or meniscal repair) with 12 weeks of exercise therapy (neuromuscular exercises 1-2 times weekly) with the option of surgery later if needed. Both RCTs found that both groups experienced clinically relevant improvements in pain and function with no clinically important differences between groups.[47,77] In both RCTs, patients with severe displaced tears (ie, locked knee indicative of displaced bucket-handle tear) and those associated with an anterior cruciate ligament rupture were excluded, as these cases typically have more aggravating symptoms and require surgery.

Meniscal repair is an arthroscopic option for traumatic tears when the tear involves the peripheral vascularized tissue (ie, outer 10%-30% of the meniscus) in an otherwise healthy meniscus.[78] A systematic review of 7 studies (1 RCT, 6 retrospective) of 367 patients comparing meniscal repair and meniscectomy found mixed results: superior self-reported function in those who had meniscal repair on one instrument and equivocal results on another.[79] Meniscal repair was associated with a 14.8% (95% CI, 11.3%-18.3%) failure rate as reported by a meta-analysis of 38 studies (1358 patients).[80]

For degenerative meniscal tears, exercise therapy is first-line treatment, with few additional benefits from surgery. A meta-analysis demonstrated that partial meniscectomy for degenerative meniscal tears resulted in slightly lower pain scores at 6 to 12 months compared with exercise therapy (5 RCTs, 943 patients; SMD, −0.22; 95% CI, −0.40 to −0.03) but no improvement compared with sham surgery (1 RCT, 146 patients; SMD, −0.08; 95% CI, −0.41 to 0.24).[48] Results were consistent at 5-year follow-up.[81] While certain subgroups of patients may benefit from partial meniscectomy, often thought to be those with mechanical symptoms, secondary analyses from RCTs demonstrate that the presence of mechanical symptoms was not associated with improved pain relief.[82,83]

Predicting patient prognosis with nonoperative or operative management is challenging. First undergoing nonoperative management for 4 to 6 weeks is appropriate for most simple traumatic

© 2023 American Medical Association. All rights reserved.

and degenerative tears. A systematic review (32 studies, 4250 patients) found that a long duration of symptoms (>1 year), radiographic OA and resection of greater than 50% of the meniscus were associated with worse clinical outcomes after partial meniscectomy; sex, onset of symptoms (acute vs chronic), tear type, and preoperative activity level were not associated with worse outcomes.[84]

The prognosis for most traumatic meniscal tears is favorable. Systematic reviews report that 80% to 87% of athletes return to preinjury sports competition following meniscal surgery[85] and do so 7 to 9 weeks after partial meniscectomy and 5 to 6 months after meniscal repair.[86] There was no difference in ability to participate in sports among patients receiving either type of management in 2 RCTs studying surgical and nonsurgical management.[47,77] However, in the long term, meniscal tears increase the risk of incident OA. A meta-analysis of 26 studies of 83 267 people found a pooled OR for OA after traumatic meniscal tear of 6.33 (95% CI, 3.81-10.50) compared with noninjured controls.[87] Highlighting the importance of preserving the meniscus when possible, a retrospective analysis of approximately 25.5 million orthopedic patients from a US insurance database found that the 114 194 patients undergoing partial meniscectomy demonstrated a greater propensity to need future knee arthroplasty (11.4%) compared with the 176 407 patients with a meniscal tear treated nonoperatively (9.5%).[88] Prognosis for degenerative meniscal tears depends on the nature of the coexisting OA. There is no evidence to suggest that the presence of a degenerative meniscal tear influences responsiveness to knee OA interventions.

Limitations

This Review has several limitations. First, quality of included literature was not evaluated. Second, the literature was not systematically reviewed and the search may have missed some relevant publications. Third, some guidelines and consensus statements were included, but these were limited to those which were informed by appropriate evidence (eg, literature review) and not exclusively based on expert opinion.

Conclusions

Knee OA, PFP, and meniscal tears are common causes of knee pain, can be diagnosed clinically, and can be associated with significant disability. First-line treatment for each condition consists of conservative management, with a focus on exercise, education, and self-management.

ARTICLE INFORMATION

Accepted for Publication: September 12, 2023.

Author Affiliations: Sydney Musculoskeletal Health, Kolling Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia (Duong, Oo, Hunter); Department of Physical Medicine and Rehabilitation, Mandalay General Hospital, University of Medicine, Mandalay, Mandalay, Myanmar (Oo); Clinical Research Centre, Zhujiang Hospital, Southern Medical University, Guangzhou, China (Ding, Hunter); Clinical Research Centre, Guangzhou First People's Hospital, School of Medicine, South China University of Technology, Guangzhou, China (Ding); La Trobe Sport and Exercise Medicine Research Centre, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Australia (Culvenor); Australian IOC Research Centre, La Trobe University, Melbourne, Australia (Culvenor); Rheumatology Department, Royal North Shore Hospital, St Leonards, Australia (Hunter).

Author Contributions: Drs Duong and Oo contributed equally as joint first authors and Drs Culvenor and Hunter served as co–senior authors.

Conflict of Interest Disclosures: Dr Hunter reported being the codirector of the Sydney Musculoskeletal Health Flagship; being editor of the osteoarthritis section for UpToDate and co-editor in chief of *Osteoarthritis and Cartilage*; and providing consulting advice on scientific advisory boards for Pfizer, Lilly, TLCBio, Novartis, TissueGene, and Biobone. No other disclosures were reported.

Funding/Support: Dr Ding received grants from the National Natural Science Foundation of China (awards 82373653 and 81974342). Dr Culvenor is a recipient of a National Health and Medical Research Council (NHMRC) of Australia Investigator Grant (award GNT2008523). Dr Hunter is employed by the University of Sydney and Royal North Shore Hospital; his salary support for the University of Sydney is supported by Arthritis Australia and an NHMRC Investigator Grant Leadership 2 (award 1194737).

Role of the Funder/Sponsor: The supporters had no role in preparation, review, or approval of the manuscript or decision to submit the manuscript for publication.

Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

REFERENCES

1. Frese T, Peyton L, Mahlmeister J, Sandholzer H. Knee pain as the reason for encounter in general practice. *ISRN Family Med*. Published online December 26, 2013. doi:10.5402/2013/930825

2. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine*. 2020;29-30:100587. doi:10.1016/j.eclinm.2020.100587

3. Smith BE, Selfe J, Thacker D, et al. Incidence and prevalence of patellofemoral pain: a systematic review and meta-analysis. *PLoS One*. 2018;13(1):e0190892. doi:10.1371/journal.pone.0190892

4. Logerstedt DS, Scalzitti DA, Bennell KL, et al. Knee pain and mobility impairments: meniscal and articular cartilage lesions revision 2018. *J Orthop Sports Phys Ther*. 2018;48(2):A1-A50. doi:10.2519/jospt.2018.0301

5. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393(10182):1745-1759. doi:10.1016/S0140-6736(19)30417-9

6. Oo WM, Linklater JM, Hunter DJ. Imaging in knee osteoarthritis. *Curr Opin Rheumatol*. 2017;29(1):86-95. doi:10.1097/BOR.0000000000000350

7. Li J, Fu S, Gong Z, et al. MRI-based texture analysis of infrapatellar fat pad to predict knee osteoarthritis incidence. *Radiology*. 2022;304(3):611-621. doi:10.1148/radiol.212009

8. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*. 2013;21(9):1145-1153. doi:10.1016/j.joca.2013.03.018

9. Hawker GA, Stewart L, French MR, et al. Understanding the pain experience in hip and knee osteoarthritis—an OARSI/OMERACT initiative. *Osteoarthritis Cartilage*. 2008;16(4):415-422. doi:10.1016/j.joca.2007.12.017

10. Carlesso LC, Law LF, Wang N, Nevitt M, Lewis CE, Neogi T; Multicenter Osteoarthritis Study Group. Association of pain sensitization and conditioned pain modulation to pain patterns in knee osteoarthritis. *Arthritis Care Res (Hoboken)*. 2022;74(1):107-112. doi:10.1002/acr.24437

11. Murphy L, Schwartz TA, Helmick CG, et al. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Rheum*. 2008;59(9):1207-1213. doi:10.1002/art.24021

12. Nelson AE, Hu D, Arbeeva L, et al. The prevalence of knee symptoms, radiographic, and symptomatic osteoarthritis at four time points: the Johnston County Osteoarthritis Project, 1999-2018. *ACR Open Rheumatol*. 2021;3(8):558-565. doi:10.1002/acr2.11295

13. Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(4):507-515. doi:10.1016/j.joca.2014.11.019

14. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. *Best Pract Res Clin Rheumatol*. 2014;28(1):5-15. doi:10.1016/j.berh.2014.01.004

15. Tanamas S, Hanna FS, Cicuttini FM, Wluka AE, Berry P, Urquhart DM. Does knee malalignment increase the risk of development and progression of knee osteoarthritis? a systematic review. *Arthritis Rheum*. 2009;61(4):459-467. doi:10.1002/art.24336

© 2023 American Medical Association. All rights reserved.

16. Øiestad BE, Juhl CB, Culvenor AG, Berg B, Thorlund JB. Knee extensor muscle weakness is a risk factor for the development of knee osteoarthritis: an updated systematic review and meta-analysis including 46 819 men and women. *Br J Sports Med*. 2022;56(6):349-355. doi:10.1136/bjsports-2021-104861

17. Vos T, Allen C, Arora M, et al; GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388(10053):1545-1602. doi:10.1016/S0140-6736(16)31678-6

18. Zhang W, Doherty M, Peat G, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis*. 2010;69(3):483-489. doi:10.1136/ard.2009.113100

19. King LK, Epstein J, Cross M, et al. Endorsement of the domains of knee and hip osteoarthritis (OA) flare: a report from the OMERACT 2020 inaugural virtual consensus vote from the flares in OA working group. *Semin Arthritis Rheum*. 2021;51(3):618-622. doi:10.1016/j.semarthrit.2021.03.010

20. Hunter DJ, McDougall JJ, Keefe FJ. The symptoms of osteoarthritis and the genesis of pain. *Med Clin North Am*. 2009;93(1):83-100. doi:10.1016/j.mcna.2008.08.008

21. National Institute for Health and Care Excellence. *Osteoarthritis in Over 16s: Diagnosis and Management*. National Institute for Health and Care Excellence; October 19, 2022.

22. Sakellariou G, Conaghan PG, Zhang W, et al. EULAR recommendations for the use of imaging in the clinical management of peripheral joint osteoarthritis. *Ann Rheum Dis*. 2017;76(9):1484-1494. doi:10.1136/annrheumdis-2016-210815

23. Youlden DJ, Dannaway J, Enke O. Radiographic severity of knee osteoarthritis and its relationship to outcome post total knee arthroplasty: a systematic review. *ANZ J Surg*. 2020;90(3):237-242. doi:10.1111/ans.15343

24. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019;27(11):1578-1589. doi:10.1016/j.joca.2019.06.011

25. Oo WM, Hunter DJ. Repurposed and investigational disease-modifying drugs in osteoarthritis (DMOADs). *Ther Adv Musculoskelet Dis*. 2022;14:1759720X221090297. doi:10.1177/1759720X221090297

26. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)*. 2020;72(2):149-162. doi:10.1002/acr.24131

27. Brophy RH, Fillingham YA. AAOS clinical practice guideline summary: management of osteoarthritis of the knee (nonarthroplasty), third edition. *J Am Acad Orthop Surg*. 2022;30(9):e721-e729. doi:10.5435/JAAOS-D-21-01233

28. Goff AJ, De Oliveira Silva D, Merolli M, Bell EC, Crossley KM, Barton CJ. Patient education improves pain and function in people with knee osteoarthritis with better effects when combined with exercise therapy: a systematic review. *J Physiother*. 2021;67(3):177-189. doi:10.1016/j.jphys.2021.06.011

29. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Br J Sports Med*. 2015;49(24):1554-1557. doi:10.1136/bjsports-2015-095424

30. Chu IJH, Lim AYT, Ng CLW. Effects of meaningful weight loss beyond symptomatic relief in adults with knee osteoarthritis and obesity: a systematic review and meta-analysis. *Obes Rev*. 2018;19(11):1597-1607. doi:10.1111/obr.12726

31. Cudejko T, van der Esch M, van der Leeden M, et al. Effect of soft braces on pain and physical function in patients with knee osteoarthritis: systematic review with meta-analyses. *Arch Phys Med Rehabil*. 2018;99(1):153-163. doi:10.1016/j.apmr.2017.04.029

32. Leopoldino AO, Machado GC, Ferreira PH, et al. Paracetamol versus placebo for knee and hip osteoarthritis. *Cochrane Database Syst Rev*. 2019;2(2):CD013273. doi:10.1002/14651858.CD013273

33. Zeng C, Doherty M, Persson MSM, et al. Comparative efficacy and safety of acetaminophen, topical and oral non-steroidal anti-inflammatory drugs for knee osteoarthritis: evidence from a network meta-analysis of randomized controlled trials and real-world data. *Osteoarthritis Cartilage*. 2021;29(9):1242-1251. doi:10.1016/j.joca.2021.06.004

34. Osani MC, Vaysbrot EE, Zhou M, McAlindon TE, Bannuru RR. Duration of symptom relief and early trajectory of adverse events for oral nonsteroidal antiinflammatory drugs in knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2020;72(5):641-651. doi:10.1002/acr.23884

35. Oo WM, Hunter J. Intra-articular therapies for knee osteoarthritis: current update. *Curr Treatm Opt Rheumatol*. 2023;9:99-119. doi:10.1007/s40674-023-00207-x

36. Concoff A, Sancheti P, Niazi F, Shaw P, Rosen J. The efficacy of multiple versus single hyaluronic acid injections: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2017;18(1):542. doi:10.1186/s12891-017-1897-2

37. Sayah SM, Karunaratne S, Beckenkamp PR, et al. Clinical course of pain and function following total knee arthroplasty: a systematic review and meta-regression. *J Arthroplasty*. 2021;36(12):3993-4002. doi:10.1016/j.arth.2021.06.019

38. Verhagen AP, Ferreira M, Reijneveld-van de Vendel EAE, et al. Do we need another trial on exercise in patients with knee osteoarthritis? no new trials on exercise in knee OA. *Osteoarthritis Cartilage*. 2019;27(9):1266-1269. doi:10.1016/j.joca.2019.04.020

39. Najm A, Alunno A, Gwinnutt JM, Weill C, Berenbaum F. Efficacy of intra-articular corticosteroid injections in knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Joint Bone Spine*. 2021;88(4):105198. doi:10.1016/j.jbspin.2021.105198

40. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? a systematic review of prospective studies in unselected patients. *BMJ Open*. 2012;2(1):e000435. doi:10.1136/bmjopen-2011-000435

41. Wylde V, Beswick A, Bruce J, Blom A, Howells N, Gooberman-Hill R. Chronic pain after total knee arthroplasty. *EFORT Open Rev*. 2018;3(8):461-470. doi:10.1302/2058-5241.3.180004

42. Nunes GS, Stapait EL, Kirsten MH, de Noronha M, Santos GM. Clinical test for diagnosis of patellofemoral pain syndrome: systematic review with meta-analysis. *Phys Ther Sport*. 2013;14(1):54-59. doi:10.1016/j.ptsp.2012.11.003

43. Solomon DH, Simel DL, Bates DW, Katz JN, Schaffer JL. The rational clinical examination. Does this patient have a torn meniscus or ligament of the knee? value of the physical examination. *JAMA*. 2001;286(13):1610-1620. doi:10.1001/jama.286.13.1610

44. Smith BE, Thacker D, Crewesmith A, Hall M. Special tests for assessing meniscal tears within the knee: a systematic review and meta-analysis. *Evid Based Med*. 2015;20(3):88-97. doi:10.1136/ebmed-2014-110160

45. Phelan N, Rowland P, Galvin R, O'Byrne JM. A systematic review and meta-analysis of the diagnostic accuracy of MRI for suspected ACL and meniscal tears of the knee. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(5):1525-1539. doi:10.1007/s00167-015-3861-8

46. van der Heijden RA, Lankhorst NE, van Linschoten R, Bierma-Zeinstra SM, van Middelkoop M. Exercise for treating patellofemoral pain syndrome. *Cochrane Database Syst Rev*. 2015;1:CD010387.

47. Skou ST, Holmich P, Lind M, et al. Early surgery or exercise and education for meniscal tears in young adults. *NEJM Evid*. 2022;1(2):1-12. doi:10.1056/EVIDoa2100038

48. Abram SGF, Hopewell S, Monk AP, Bayliss LE, Beard DJ, Price AJ. Arthroscopic partial meniscectomy for meniscal tears of the knee: a systematic review and meta-analysis. *Br J Sports Med*. 2020;54(11):652-663. doi:10.1136/bjsports-2018-100223

49. Thorlund JB, Juhl CB, Roos EM, Lohmander LS. Arthroscopic surgery for degenerative knee: systematic review and meta-analysis of benefits and harms. *BMJ*. 2015;350:h2747. doi:10.1136/bmj.h2747

50. Powers CM, Witvrouw E, Davis IS, Crossley KM. Evidence-based framework for a pathomechanical model of patellofemoral pain: 2017 patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, UK: part 3. *Br J Sports Med*. 2017;51(24):1713-1723. doi:10.1136/bjsports-2017-098717

51. Rothermich MA, Glaviano NR, Li J, Hart JM. Patellofemoral pain: epidemiology, pathophysiology, and treatment options. *Clin Sports Med*. 2015;34(2):313-327. doi:10.1016/j.csm.2014.12.011

52. Dye SF. The pathophysiology of patellofemoral pain: a tissue homeostasis perspective. *Clin Orthop Relat Res*. 2005;(436):100-110. doi:10.1097/01.blo.0000172303.74414.7d

53. Crossley KM, van Middelkoop M, Callaghan MJ, Collins NJ, Rathleff MS, Barton CJ. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions).

© 2023 American Medical Association. All rights reserved.

Br J Sports Med. 2016;50(14):844-852. doi:10.1136/bjsports-2016-096268

54. Lankhorst NE, van Middelkoop M, Crossley KM, et al. Factors that predict a poor outcome 5-8 years after the diagnosis of patellofemoral pain: a multicentre observational analysis. *Br J Sports Med*. 2016;50(14):881-886. doi:10.1136/bjsports-2015-094664

55. Neal BS, Lack SD, Lankhorst NE, Raye A, Morrissey D, van Middelkoop M. Risk factors for patellofemoral pain: a systematic review and meta-analysis. *Br J Sports Med*. 2019;53(5):270-281. doi:10.1136/bjsports-2017-098890

56. Crossley KM, Callaghan MJ, van Linschoten R. Patellofemoral pain. *BMJ*. 2015;351:h3939. doi:10.1136/bmj.h3939

57. Basha MAA, Eldib DB, Aly SA, et al. Diagnostic accuracy of ultrasonography in the assessment of anterior knee pain. *Insights Imaging*. 2020;11(1):107. doi:10.1186/s13244-020-00914-2

58. Eijkenboom JFA, Waarsing JH, Oei EHG, Bierma-Zeinstra SMA, van Middelkoop M. Is patellofemoral pain a precursor to osteoarthritis? patellofemoral osteoarthritis and patellofemoral pain patients share aberrant patellar shape compared with healthy controls. *Bone Joint Res*. 2018;7(9):541-547. doi:10.1302/2046-3758.79.BJR-2018-0112.R1

59. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *BMJ*. 2008;337:a1735.

60. Logan CA, Bhashyam AR, Tisosky AJ, et al. Systematic review of the effect of taping techniques on patellofemoral pain syndrome. *Sports Health*. 2017;9(5):456-461. doi:10.1177/1941738117710938

61. Collins NJ, Barton CJ, van Middelkoop M, et al. 2018 Consensus statement on exercise therapy and physical interventions (orthoses, taping and manual therapy) to treat patellofemoral pain: recommendations from the 5th International Patellofemoral Pain Research Retreat, Gold Coast, Australia, 2017. *Br J Sports Med*. 2018;52(18):1170-1178. doi:10.1136/bjsports-2018-099397

62. Macri EM, Hart HF, Thwaites D, et al. Medical interventions for patellofemoral pain and patellofemoral osteoarthritis: a systematic review. *J Clin Med*. 2020;9(11):3397. doi:10.3390/jcm9113397

63. Hinman RS, Lentzos J, Vicenzino B, Crossley KM. Is patellofemoral osteoarthritis common in middle-aged people with chronic patellofemoral pain? *Arthritis Care Res (Hoboken)*. 2014;66(8):1252-1257. doi:10.1002/acr.22274

64. Collins NJ, Bierma-Zeinstra SM, Crossley KM, van Linschoten RL, Vicenzino B, van Middelkoop M. Prognostic factors for patellofemoral pain: a multicentre observational analysis. *Br J Sports Med*. 2013;47(4):227-233. doi:10.1136/bjsports-2012-091696

65. Walker PS, Erkman MJ. The role of the menisci in force transmission across the knee. *Clin Orthop Relat Res*. 1975;(109):184-192. doi:10.1097/00003086-197506000-00027

66. Peat G, Bergknut C, Frobell R, Jöud A, Englund M. Population-wide incidence estimates for soft tissue knee injuries presenting to healthcare in southern Sweden: data from the Skåne Healthcare Register. *Arthritis Res Ther*. 2014;16(4):R162. doi:10.1186/ar4678

67. Ulstein S, Årøen A, Engebretsen L, Forssblad M, Røtterud JH. Effect of concomitant meniscal lesions and meniscal surgery in ACL reconstruction with 5-year follow-up: a nationwide prospective cohort study from Norway and Sweden of 8408 patients. *Orthop J Sports Med*. 2021;9(10):23259671211038375. doi:10.1177/23259671211038375

68. Englund M, Guermazi A, Gale D, et al. Incidental meniscal findings on knee MRI in middle-aged and elderly persons. *N Engl J Med*. 2008;359(11):1108-1115. doi:10.1056/NEJMoa0800777

69. Culvenor AG, Øiestad BE, Hart HF, Stefanik JJ, Guermazi A, Crossley KM. Prevalence of knee osteoarthritis features on magnetic resonance imaging in asymptomatic uninjured adults: a systematic review and meta-analysis. *Br J Sports Med*. 2019;53(20):1268-1278. doi:10.1136/bjsports-2018-099257

70. Snoeker BAM, Bakker EWP, Kegel CAT, Lucas C. Risk factors for meniscal tears: a systematic review including meta-analysis. *J Orthop Sports Phys Ther*. 2013;43(6):352-367. doi:10.2519/jospt.2013.4295

71. McHugh CG, Matzkin EG, Katz JN. Mechanical symptoms and meniscal tear: a reappraisal. *Osteoarthritis Cartilage*. 2022;30(2):178-183. doi:10.1016/j.joca.2021.09.009

72. Beaufils P, Becker R, Kopf S, et al. Surgical management of degenerative meniscus lesions: the 2016 ESSKA meniscus consensus. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(2):335-346. doi:10.1007/s00167-016-4407-4

73. Kocabey Y, Tetik O, Isbell WM, Atay OA, Johnson DL. The value of clinical examination versus magnetic resonance imaging in the diagnosis of meniscal tears and anterior cruciate ligament rupture. *Arthroscopy*. 2004;20(7):696-700. doi:10.1016/S0749-8063(04)00593-6

74. Madhusudhan TR, Kumar TM, Bastawrous SS, Sinha A. Clinical examination, MRI and arthroscopy in meniscal and ligamentous knee injuries—a prospective study. *J Orthop Surg Res*. 2008;3:19. doi:10.1186/1749-799X-3-19

75. Abram SGF, Beard DJ, Price AJ; BASK Meniscal Working Group. Arthroscopic meniscal surgery: a national society treatment guideline and consensus statement. *Bone Joint J*. 2019;101-B(6):652-659. doi:10.1302/0301-620X.101B6.BJJ-2019-0126.R1

76. Bleakley C, McDonough S, MacAuley D. The use of ice in the treatment of acute soft-tissue injury: a systematic review of randomized controlled trials. *Am J Sports Med*. 2004;32(1):251-261. doi:10.1177/0363546503260757

77. van der Graaff SJA, Eijgenraam SM, Meuffels DE, et al. Arthroscopic partial meniscectomy versus physical therapy for traumatic meniscal tears in a young study population: a randomised controlled trial. *Br J Sports Med*. 2022;56(15):870-876. doi:10.1136/bjsports-2021-105059

78. Gerritsen LM, van der Lelij TJN, van Schie P, et al. Higher healing rate after meniscal repair with concomitant ACL reconstruction for tears located in vascular zone 1 compared to zone 2: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc*. 2022;30(6):1976-1989. doi:10.1007/s00167-022-06862-2

79. Xu C, Zhao J. A meta-analysis comparing meniscal repair with meniscectomy in the treatment of meniscal tears: the more meniscus, the better outcome? *Knee Surg Sports Traumatol Arthrosc*. 2015;23(1):164-170. doi:10.1007/s00167-013-2528-6

80. Costa GG, Grassi A, Zocco G, et al. What is the failure rate after arthroscopic repair of bucket-handle meniscal tears? a systematic review and meta-analysis. *Am J Sports Med*. 2022;50(6):1742-1752. doi:10.1177/03635465211015425

81. Fernández-Matías R, García-Pérez F, Gavín-González C, Martínez-Martín J, Valencia-García H, Flórez-García MT. Effectiveness of exercise versus arthroscopic partial meniscectomy plus exercise in the management of degenerative meniscal tears at 5-year follow-up: a systematic review and meta-analysis. *Arch Orthop Trauma Surg*. 2023;143(5):2609-2620. doi:10.1007/s00402-022-04579-y

82. MacFarlane LA, Yang H, Collins JE, et al. Association between baseline meniscal symptoms and outcomes of operative and nonoperative treatment of meniscal tear in patients with osteoarthritis. *Arthritis Care Res (Hoboken)*. 2022;74(8):1384-1390. doi:10.1002/acr.24588

83. Sihvonen R, Englund M, Turkiewicz A, Järvinen TL; Finnish Degenerative Meniscal Lesion Study Group. Mechanical symptoms and arthroscopic partial meniscectomy in patients with degenerative meniscus tear: a secondary analysis of a randomized trial. *Ann Intern Med*. 2016;164(7):449-455. doi:10.7326/M15-0899

84. Eijgenraam SM, Reijman M, Bierma-Zeinstra SMA, van Yperen DT, Meuffels DE. Can we predict the clinical outcome of arthroscopic partial meniscectomy? a systematic review. *Br J Sports Med*. 2018;52(8):514-521. doi:10.1136/bjsports-2017-097836

85. Ekhtiari S, Khan M, Kirsch JM, Thornley P, Larson CM, Bedi A. Most elite athletes return to competition following operative management of meniscal tears: a systematic review. *J ISAKOS*. 2018;3(2):110-115. doi:10.1136/jisakos-2017-000181

86. Lee YS, Lee O-S, Lee SH. Return to sports after athletes undergo meniscal surgery: a systematic review. *Clin J Sport Med*. 2019;29(1):29-36. doi:10.1097/JSM.0000000000000500

87. Poulsen E, Goncalves GH, Bricca A, Roos EM, Thorlund JB, Juhl CB. Knee osteoarthritis risk is increased 4-6 fold after knee injury—a systematic review and meta-analysis. *Br J Sports Med*. 2019;53(23):1454-1463. doi:10.1136/bjsports-2018-100022

88. Barnds B, Morris B, Mullen S, Schroeppel JP, Tarakemeh A, Vopat BG. Increased rates of knee arthroplasty and cost of patients with meniscal tears treated with arthroscopic partial meniscectomy versus non-operative management. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(7):2316-2321. doi:10.1007/s00167-019-05481-8

© 2023 American Medical Association. All rights reserved.